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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,464	07/18/2002	Catherine Anne Abbott	GH-007	7028

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EXAMINER
SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No.	Applicant(s)	
	10/070,464	ABBOTT ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *10-23 and 25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 24* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Applicant's election with traverse of Group I, Claims 1-9 and 24 in Paper No. 8 is acknowledged. The traversal is on the following ground(s). Applicant's state that the claims clearly relate to the same inventive concept, and have already been searched as evidenced by the International Preliminary Examination Report, thus no undue burden would be placed on the Examiner if these claims were to be examined together. Applicant's also state that Kawakami et al 2000, can not be used to establish the state of the art as, the reference date is after the claimed priority date of AU PQ5709. Applicants also state that the requirement for restriction is not mandatory but, is merely discretionary and that the courts have recognized the advantages of patentee claiming all aspects of their invention.

These arguments are not found persuasive for the following reasons.

As acknowledged by the applicants in Paper No. 8, restriction practice is discretionary.

MPEP 1893.03(e) says:

> If the international application underwent preliminary examination, the International Preliminary Examination Report (Form PCT/IPEA/409) reflects the International Preliminary Authority's non-binding opinion regarding novelty, inventive step and industrial applicability. The examiner may adopt any portion or all of this opinion upon consideration in the national stage so long as it is consistent with U.S. practice. The examiner should comment upon the Report in the first Office action on the merits to reflect that the Report has been considered. The comment may be a mere acknowledgement

MPEP 1893.03(d) says:

> 37 CFR 1.499. Unity of invention during the national stage
> If the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner. Review of any such requirement is provided under § § 1.143 and 1.144

Therefore, the Office is not bound by an International Search report.

It is acknowledged that the priority date of AU PQ5709 predates Kawakami et al 2000. However, the priority date used to analyze Unity of Invention for this application was the filing date, July 18, 2002, not the priority date of AU PQ5709, February 18, 2000. The protein shown in Fig 2 of AU PQ5709 appears to terminate at residue 881, which is 1 residue shorter than SEQ ID NO: 1 of this application. Therefore, it appeared that SEQ ID NO: 1 of this application was not contained in AU PQ5709. It is now acknowledged that a typo in Fig 2 of AU PQ5709 indicating that the leucine residue at the first position on the last line of the protein sequence is Leu^{864}, lead the examiner to deduce that said protein terminated at Ile^{881}. It is also acknowledged that applicants have now supplied a certified ribbon copy of priority document AU PQ 2762 filed September 10, 1999. Therefore, the priority date of September 10, 1999 is established for this application.

Nonetheless, the inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: The technical feature linking Groups I-VII appears to be that they all relate to prolyloligo dipeptidyl peptidases. However, Sprague et al, 1990 teach the cloning and expression of a gene, STE13, encoding a dipeptidyl aminopeptidase, that will degrade proteins by releasing alamine-proline dipeptide or X-protein, where X is any amino acid, from the amino-terminus (Col 3, lines 11-16). Therefore Groups I-VII share no special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Additional reasons for lack of unity are described in the prior action on page 2, lines 14-35.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-27 are pending. Claims 1-9 and 24 are examined on their merits.

Specification-Objections

The abstract is objected to for not describing the invention of this application. Correction is required.

The specification is objected to for not providing a sequence listing providing sequence identifier numbers (SEQ ID NO: X) for the sequence recited in Claim 1. A new sequence listing including the sequences HisGlyTrpSerTyrGlyGlyTyrLeu, LeuAspGluAsnValHisPheAlaHis, GluArgHisSerIleArg, and PheValLeuGlnGluGluPhe is required.

Claims-Objections

Claim 1 is objected to for reciting "...the sequence which has at least 60% identity...". "...the sequence..." lacks antecedent basis and should be amended to "...a sequence ...".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1, as written, encompasses naturally occurring cellular proteins Such proteins are non-statutory, not showing the "hand of man" and, thus, Claim 1 is rejected under 35 U.S.C. 101. It is suggest that Claim 1 be amended to recite "An isolated peptide..."

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 1, 4, and 8, the phrase "... which has the substrate specificity of the sequence shown in SEQ ID NO: 1..." has two interpretations. The phrase could mean either the peptide being recited has the polypeptide set forth by SEQ ID NO: 1 as a substrate or the peptide being recited has the same substrate as the polypeptide set forth by SEQ ID NO: 1. As dependent claims, Claims 2, 3, 5-9, and 24 are rejected for the same reasons. For purposes of examination, it was assumed that the Claims 1, 4, and 8 are meant to recite that the peptides have the same substrate specificity as the protease set forth by SEQ ID NO: 1. Correction is required.

Claims 1, 6, 7, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, without a sequence identifier number (SEQ ID NO: X), reciting amino acid residue designations His^{736}, Leu^{816}, Glu^{847}, and Phe^{255} is indefinite. It is unclear whether or not the recited peptides must be present in a larger protein at the indicated amino acid position numbers; if not, such designations are unnecessary. For purposes of examination, it was assumed that the peptides do have to be present in a larger protein but, not at the indicated positions. It is suggested that Claim 1 be amended to designate the recited peptides by sequence identifier numbers (SEQ ID NO: X).

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 6, 7, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein set forth by SEQ ID NO: 1, does not reasonably provide enablement for any peptide which comprises the sequences HGWSYGGYL, LDENVHFAH, ERHSIR, and FVLNEEF which has the same substrate specificity as the protein set forth by SEQ ID NO: 1 or any peptide that has at least 60% identity with SEQ ID NO: 1 and has the same substrate specificity as the protein set forth by SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass any peptide which comprises the sequences HGWSYGGYL, LDENVHFAH, ERHSIR, and FVLNEEF which has the same substrate specificity as the protein set forth by SEQ ID NO: 1. Claim 1 is so broad as to also encompass any peptide which has at least 60% identity with SEQ ID NO: 1 and has the same substrate specificity as the protein set forth by SEQ ID NO: 1. Claim 2 is so broad as to encompass the peptides of Claim 1 having at least 75% identity with SEQ ID NO: 1. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired prolyloligo depeptidyl peptidase activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e.

expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claim 1 which, encompasses all peptides which comprise the sequences HGWSYGGYL, LDENVHFAH, ERHSIR, and FVLNEEF which have the same substrate specificity as the protein set forth by SEQ ID NO: 1 and all peptides that have at least 60% identity with SEQ ID NO: 1 and have the same substrate specificity as the protein set forth by SEQ ID NO: 1. The specification does not support the broad scope of the Claim 2 which, encompasses the peptides of Claim 1 having 75% identity with SEQ ID NO: 1. The specification does not support the broad scope of Claims 1 and 2 because the specification does not establish: (A) regions of the peptide structure which may be modified without effecting the peptidase activity; (B) the general tolerance of the activity of the peptidase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D)

the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 6, 7, and 24 recite further derivatives, location within the cell, and compositions comprising the peptides recited in Claim 1, Claims 6, 7, and 24 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of peptidases with an enormous number of amino acid modifications of the peptidase of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 2, 6, 7, and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of peptide derivatives of the protein set forth by SEQ ID NO: 1 having prolyloligo depeptidyl peptidase activity. The specification teaches the structure of only a single representative species of such proteins. Moreover, the specification

fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a prolyloligo depeptidyl peptidase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope